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Sent: Monday, September 19, 2005 1:31 PM
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Afternoon Mike,

Thanks for speaking to me earlier today. As promised, I am forwarding 3 documents to assist in the PBT classification of 2 phthalate esters (DIDP and DnHP) currently being considered under the Washington State PBT rule.

"Comments on Washington State Dept Ecology PBT list for DIDP" was prepared to comment specifically on the inclusion of DIDP on the PBT list as discussed in Summary of Ecology's Response to Comments on the PBT Rule (Sep2005). It comments on the data used by Ecology and cites appropriate data to characterize P and B. It also identifies an incorrect SMILES notation used by the PBT Profiler model that Ecology applied to estimate persistence for DIDP. A more representative SMILES notation for DIDP (CAS 68515-49-1) is: O=C(c1ccccc1C(=O)OCCCCCCCC(C)C)OCCCCCCCC(C)C
The use of structures to correctly model DIDP is briefly discussed in the document, but a representative structure was not provided. Although the structure above is considered appropriate for DIDP, there are measured biodegradation data (unpublished) described in the document that are more appropriate to assess P.

"The ACC DSL PE PBT Final Report" (Aug 2004) is a document that was recently prepared for Environment Canada (EC) for a wider range of substances including selected phthalate esters.The phthalate esters reviewed include DIDP, and although DnHP is not specifically addressed, there are data that can be used as read-across. Under the Canadian Environmental Protection Act of 1999, EC was required to assess all substances on the Canadian Domestic Substances List (DSL) with respect to P,B, and iT (inherent toxicity). EC provisionally categorized selected substances on the DSL and the report was prepared to provide a review of available data to support an appropriate PBiT categorization of several substances including phthalates based on criteria established by EC, which are different than those applied by Ecology. However, this report is provided as additional information The review was conducted in order to:

- Complete a critical evaluation using data from the literature, unpublished industry studies, and "read-across" principles as appropriate.
- Provide a comparison of recommended PBiT assessments to those initially proposed by EC.
- Identify substances for which available information support a PBiT, PiT, or BiT categorization.

The "HMWPE (High Molecular Weight Phthalate Ester) Category SIAP (SIDS Information Assessment Profile) Final OECD Clean - SIAM (SIDS Information Assessment Meeting) 19" is a document agreed to by member countries of OECD (Oct 2004) that summarizes selected data for various endpoints including B. Although the category did not include DIDP specifically, as it had already been risk assessed by the European Union, the range of phthalate esters included in the category covered a range that included DIDP. The HMWPE Category ranged from a C7-9 to a C13 phthalate ester. This document has been published by OECD, but the supporting documents are still being finalized and are not publically available as yet. However, the conclusion for B made by OECD Member States, which includes the U.S. and Canada, is as follows:

"Finally, it has been demonstrated that HMWPEs have a low potential to bioaccumulate in aquatic species, demonstrated by a food web study on DINP, and bioconcentration studies on DINP, DIUP and di-C13 PE. Metabolic transformation is the most likely reason why these substances exhibit decreasing concentrations from lower to higher trophic levels."

Please feel free to call me to discuss any of the information contained in these docuemnts.

Regards,
Douglas

(See attached file: Comments on Washington State Dept Ecology PBT List for DIDP.doc)

(See attached file: ACC DSL PE PBT Final Report rev23Aug04.doc)

(See attached file: HMWPE_Category_SIAP_FINAL OECD Clean - SIAM 19 - 26Oct04.doc)

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AN ASSESSMENT OF THE PERSISTENCE, BIOACCUMULATION, AND INHERENT TOXICITY OF SELECTED PHTHALATES, TRIMELLITATES, ADIPATES, AND RELATED MONOESTERS ON THE CANADIAN DOMESTIC SUBSTANCE LIST (DSL)

Prepared for the Phthalate Esters Panel
of the American Chemistry Council

By
Tom Parkerton
Douglas Winkelmann
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August 9, 2004

I. Executive Summary

Under the Canadian Environmental Protection Act of 1999, Environment Canada (EC) is required to assess all substances on the Canadian Domestic Substances List (DSL) with respect to persistence, bioaccumulation, and inherent toxicity (PBiT). EC has provisionally categorized selected substances on the DSL for PBiT and is soliciting further data to improve the technical basis of this initial assessment. This report provides a review of available data that supports PBiT categorization of 93 selected phthalates, trimellitates, adipates, and related monoesters on the DSL based on criteria established by EC. EC has not completed its evaluation of all 93 substances, leaving some of the endpoints as "not assessed" or "uncertain". This review was conducted in order to:

- Complete a critical evaluation of all 93 substances using data from the literature, unpublished industry studies, and "read across" principles as appropriate.
- Provide a comparison of recommended PBiT assessments for all 93 substances based on this evaluation to those initially proposed by EC.
- Identify substances for which available information provided in this technical review support PBiT, PiT, or BiT categorization.

This review identified 3 substances that are modeled to meet the EC criteria for P, 4 substances that are modeled to meet the criteria for B, and 15 substances that meet the criteria for iT based on available ecotoxicity data or analogy via read-across principles. One substance, *1,2-benzenedicarboxylic acid, dicyclohexyl ester* (CAS# 84617), was identified as potentially meeting both B and iT criteria. No substance was identified as a PiT or PBiT.

II. Scope & Objectives

The Canadian Environmental Protection Act of 1999 has mandated the categorization of substances on the Canadian Domestic Substance List (DSL) with respect to persistence, bioaccumulation, and inherent toxicity (i.e., PBiT) properties by September 14, 2006. Environment Canada (EC) has published technical guidelines describing the systematic approach that is to be used for this categorization process.[1] EC has subsequently applied this scheme to preliminarily categorize 10,629 organic substance into five color-coded classes for prioritization and is seeking comments and additional supporting P, B, and iT data on substances included in this initial assessment. EC has also identified a list of over 4,234 unknown or variable composition, complex reaction products or biological materials (UVCBs) that have not been assessed but for which technical input is also being solicited.

For over several decades, the Phthalate Ester Panel (Panel) of the American Chemistry Council and its member companies have actively been engaged in environmental fate and effects research on phthalate esters. While phthalate esters are the principal focus of the Panel, trimellitate and adipate plasticizers are also included in the scope of Panel efforts. Consequently, Panel members can contribute data and expertise relevant to environmental assessment of these substance classes.

The objective of this report is to provide a technical review of the PBiT properties of selected phthalates, trimellitates, and adipates. The report will highlight the availability of measured data that either confirms EC's preliminary categorization or indicates that revisions are warranted. In addition, recommendations on the PBiT properties of substances from these classes that have been designated as UVCBs will also be presented. A summary of EC's preliminary assessment of these substances is shown in Table 1.

Table 1. Preliminary Categorization of Selected Phthalates, Trimellitates, and Adipates.

Quantity	<1 tonne	1 to <1000 tonnes	>=1000 tonnes
Categorization "in" based on experimental data	2	0	1
Categorization "in" based on QSAR data	5	5	3
Uncertain - model difficult iT, B (Gobas only)	10	3	4
P, B, not iT eco organisms	7		
Not P not B	25		
Not assessed (UVCBs)	28		
TOTAL	*93*		

III. Substance Description

Phthalate esters are an important class of industrial chemicals that have the general formula shown in Figure 1. Phthalates can be grouped based on the nature of the R groups. Dialkyl phthalate esters possess linear or branched alkyl chains that range from 1 (dimethyl phthalate) to 13 carbons (ditridecyl phthalate). Benzyl phthalates generally contain a phenylmethyl group and an alkyl chain as R groups. Although less commercially important, some phthalates contain a saturated benzene ring as an R group (i.e., cyclohexyl phthalates). The diversity in the nature of potential R groups results in an enormous range of phthalate ester physical-chemical properties supporting commercial use in numerous product applications.[2]

Phthalate esters are produced by reacting phthalic anhydride with the corresponding alcohol of the desired R group. For example, di-n-butyl phthalate is produced via reaction with n-butyl alcohol.

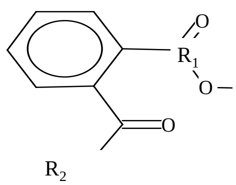

Figure 1. General Structure of Phthalate Esters.

Aliphatic alcohols used in phthalate ester synthesis are typically produced using a hydroformulation process. In this process, hydrogen, carbon monoxide, and low molecular weight olefins are reacted to form aldehydes that are then hydrogenated to yield alcohols. Since low molecular weight olefins with different branching patterns can react in various combinations, the resulting alcohols formed by this process do not have unique structures but rather represent isomeric mixtures with a defined distribution of carbon numbers. When these commercial alcohols are used in esterification, the resulting esters also exist as a mixture of isomers that reflects the composition of the parent alcohol. The isomeric nature of the alcohol used is often reflected in the nomenclature of the phthalate, e.g. 1,2-benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich, or 1,2-benzenedicarboxylic acid, di-C7-11-branched and linear alkyl esters. However, in some cases a specific alcohol is used so that a single isomer results, e.g. di-2-ethylhexyl phthalate is synthesized using 2-ethyl hexanol.

Despite the complexity of many commercial phthalates listed on the DSL, the environmental properties of the various structures within a given Chemical Abstract Services registry number (CAS #) do not vary that substantially to preclude assessment using one or several representative structures. In fact EPIWIN[*] assigns representative SMILES[**] structures for QSAR evaluation of 17 of the 18 phthalates designated as UVCBs relevant to the Panel (1,2-benzenedicarboxylic acid, mixed decyl and octyl diesters, CAS # 90193945 was the only substance with no SMILES match). Moreover, the designation of specific phthalates as UVCBs is misleading since many of the phthalates included in EC's initial categorization assessment are not unique structures but rather isomeric mixtures. For example, 1,2-benzenedicarboxylic acid, diisononyl ester (CAS # 28553120) which was among the initial list of organic substances categorized by EC, is compositionally very similar to 1,2-benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich (CAS # 68515480), which was included on EC's UVCB list. However, for the purposes of human and environmental risk assessment these substances can be treated collectively as "di-isononyl phthalate".[3] Therefore unlike other UVCBs, such as petroleum substances which contain hydrocarbon constituents with structural classes that vary significantly in physical properties and amounts within a given CAS #, commercial phthalates have relatively well defined chemical compositions and thus can be assessed as "pseudo" single substances. Therefore, while

[*] Estimation Program Interface for Windows
[**] Simplified Molecular Input Line Entry Specification

these commercial products are often structurally complex, this complexity can be adequately resolved for environmental assessment purposes given the structural similarity of the constituents.

Trimellitates are produced by esterification of trimellitic anhydride and are structurally related to phthalates but contain a third ester linkage as shown in Figure 2. All of the trimellitates on the DSL including those designated as UVCBs have linear or branched alkyl chains ranging from 1 to 10 carbons. As in the case of phthalates, commercial trimellitates are often comprised of alkyl chains with different isomers of a defined carbon length. EPIWIN provided representative SMILES structures for all five trimellitates listed as UVCBs.

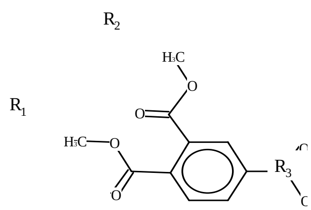

Figure 2. General Structure of Trimellitates.

While adipates share the dicarboxylic acid functionality with phthalates, this class of plasticizers is derived from a n-hexanedioic acid rather than an aromatic ring as illustrated in Figure 3. Adipates on the DSL including those designated as UVCBs have linear or branched single or isomeric alkyl chains ranging from 1 to 13 carbons as well as benzyl R groups. EPIWIN provided representative SMILES structures for two of the five adipates listed as UVCBs.

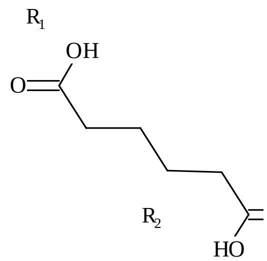

Figure 3. General Structure of Adipates.

A summary of the names, CAS #s, and preliminary categorization (if assessed) by EC of the 93 phthalates, trimellitates, and adipates that are the subject of this review are included in Appendix 1. Substances were sorted into three groups for each class based on EC's preliminary evaluation: (1) do not meet PBiT criteria; (2) potentially meet PBiT criteria and (3); UVCB substances not yet assessed. To enable QSAR evaluation, representative SMILES strings are proposed for UVCB substances that did not have a CAS # match in EPIWIN (Appendix 2). In addition, EPIWIN assigned one UVCB substance (1,2-benzenedicarboxylic acid, benzyl C7-9-branched and linear alkyl esters, CAS # 68515402) an erroneous SMILES structure. Therefore, a corrected representative structure for this substance is provided.

IV. Persistence Assessment

A provisional P assessment was performed by EC for 65 phthalates, trimellitates, and adipates. Only three of these substances were preliminarily found to meet EC's P criteria (dimethyl and diethyl phthalate and dimethyl adipate). These compounds are the most volatile members of the plasticizers reviewed and exhibit a significant presence in the atmosphere based on Level II multimedia modeling calculations. Since these compounds have predicted atmospheric half-lives of >2 days, the EC criteria for P categorization are met. None of the remaining 62 plasticizers were found to meet the P criteria consistent with the well-documented biodegradable nature of phthalates[4,5] and trimellitates/adipates (Table 2).

Table 2. Summary of Biodegradation Test Data for Adipates and Trimellitates.

CAS #	Chemical Name	Test	Duration (days)	Ultimate Degradation (%)	Reference
103-23-1	di-2-ethylhexyl adipate	OECD 301B	28	89	6
1330-86-5	di-isooctyl adipate	OECD 301 B	28	87	7
337032-08-1	di-isononyl adipate	OECD 301F	28	73	8
27178-16-1	di-isodecyl adipate	OECD 301F	28	68	9
27178-16-1	di-isodecyl adipate	OECD 301F	28	77	7
68515-75-3	di-C7-C9 branched & linear adipate	SCAS/CO2 Evolution	1	67-88	10
16958-92-2	di-isotridecyl adipate	OECD 301B	28	66	6
16958-92-2	di-isotridecyl adipate	OECD 301B	28	57	7
16958-92-2	di-isotridecyl adipate	OECD 301B	28	60	7
3319-31-1	tri-2-ethylhexyl trimellitate	Shake Flask	28	69-72	11

The remaining 28 UVCBs do not have a significant presence in air, and, therefore, P assessment depends on the estimated half-life in water / soil. The predicted half-lives derived from the Ultimate Survey Model of BIOWIN (version 4.0) for these substances are provided in Table 3.

Table 3. Summary of Estimated Half-lives for Selected Phthalates, Trimellitates, and Adipates included on EC's UVCB List Not Assessed for Persistence.

Chemical Name	CAS #	Log K_{ow}	Result	(days)
Phthalates				
1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear	68515504	6.46	2.8267	15
1,2-Benzenedicarboxylic acid, benzyl C7-9-branched and linear alkyl esters	68515402	7.15	2.6563	15
1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters,C7-rich	71888896	7.41	2.6785	37.5
1,2-Benzenedicarboxylic acid, diheptyl ester, branched and linear	68515446	7.41	2.6785	37.5
1,2-Benzenedicarboxylic acid, di-C7-11-alkyl esters	68648919	7.56	3.2752	8.67
1,2-Benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters	68648931	8.1	3.2132	15
1,2-Benzenedicarboxylic acid, heptyl nonyl ester, branched and linear	111381896	8.39	2.9148	15
1,2-Benzenedicarboxylic acid, di-C7-11-branched and linear alkyl esters	68515424	8.47	2.9148	15
1,2-Benzenedicarboxylic acid, di-C7-9-branched and linear alkyl esters	68515413	8.47	2.9148	15
1,2-Benzenedicarboxylic acid, heptyl undecyl ester, branchedand linear	111381909	9.37	2.8528	15
1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich	68515480	9.52	3.1512	15
1,2-Benzenedicarboxylic acid, dinonyl ester, branched and linear	68515457	9.52	3.1512	15
1,2-Benzenedicarboxylic acid, mixed decyl and octyl diesters	90193945	9.52	3.1512	15
1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich	68515491	10.28	2.0683	60
1,2-Benzenedicarboxylic acid, nonyl undecyl ester, branchedand linear	111381910	10.28	2.7908	15
1,2-Benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters	68515435	10.39	2.5787	37.5
1,2-Benzenedicarboxylic acid, diundecyl ester, branched andlinear	85507795	11.83	2.6978	37.5
1,2-Benzenedicarboxylic acid, di-C11-14-branched alkyl esters, C13-rich	68515479	12.25	1.9443	60
Adipates				
Hexanedioic acid,branched & linear nonyl,decyl,2-ethylhexyl,hexyl&octyl esters	132539049	6.72-10.01	2.63-3.05	15-37.5
Hexanedioic acid, di-C7-9-branched and linear alkyl esters	68515753	7.55	2.6917	37.5
Hexanoic acid, 2-ethyl-, C12-14-alkyl esters	68411869	8.65	3.2454	15
Hexanedioic acid, di-C7-9-alkyl esters	84539628	8.75	3.2263	15
Hexanedioic acid, mixed decyl and octyl diesters	90411566	10.23	3.13	15
Trimellitates				
1,2,4-Benzenetricarboxylic acid, 2-ethylhexyl ester[*]	68186312	4.12	3.1321	15
1,2,4-Benzenetricarboxylic acid, isooctyl ester[*]	68186323	4.61	2.8027	15
1,2,4-Benzenetricarboxylic acid, tri-C7-9-branched and linear alkyl esters	68515606	10.04	2.5045	37.5
1,2,4-Benzenetricarboxylic acid, mixed decyl and hexyl and octyl esters	68130507	11.81	3.3065	8.67
1,2,4-Benzenetricarboxylic acid, mixed branched tridecyl andisodecyl esters	70225057	16.08	2.4308	37.5

[*] Substance is a trimellitate monoester

With two exceptions, all 28 substances not previously assessed have estimated primary half-lives in surface water between 15 to 37.5 days and thus do not meet EC's P criteria. For the two substances with predicted half-lives of 60 days (C10 and C13 rich dialkyl phthalates), OECD ready biodegradation test data (301 F manometric respirometry) are available showing 67 and 63% ultimate biodegradation in 28 days, respectively.[12,13] Using EC (2003) guidance, these measured data translate into primary surface water half-lives of 5 days. The discrepancy between BIOWIN predictions and measured data is due to the unrepresentative SMILES structure that was assigned by EPIWIN for characterizing these substances. The EPIWIN structure that matched these CAS #'s included a terminal tertiary carbon on both alkyl chains that is known to impede biodegradation. However, these products actually consist of a mixture of largely methyl-branched isomers that are readily biodegradable.

In summary, available information supports EC's initial categorization of the 65 substances as not persistent, with the exception of dimethyl phthalate, diethyl phthalate, and dimethyl adipate as previously discussed. Evaluation of the remaining substances in these classes that were not assessed by EC (i.e., those which were included on the UVCB list) indicates these substances are also readily biodegradable and therefore do not meet P criteria.

V. Bioaccumulation Assessment

In contrast to persistence, EC provisionally characterized approximately half of the 65 "non-UVCB" substances as fulfilling the B criterion. For most of the substances, this decision was based on the default Gobas BAF (Bioaccumulation Factor) model or the Forecast BCFmax (Bioconcentration Factor) QSAR model. The Gobas BAF model categorizes all substances with Log K_{ow} between 4.1 and 12.0 as potentially bioaccumulative based on a number of conservative default assumptions including negligible metabolism. Generally, the BCFmax QSAR model yielded BCF predictions that were one to two orders of magnitude higher than the BCFwin QSAR model. A difference between these BCF models is not unexpected since the BCFmax predicts the maximum possible BCF assuming no metabolism whereas the BCFwin attempts to quantitatively take biotransformation into account via structure-specific fragment correction factors. The susceptibility of esters in general and phthalates in particular to biotransformation by aquatic organisms is well recognized.[1,14,15,16]

For a number of selected phthalates assessed, recent field-derived BAFs were used as the basis for B assessment[17]. Table 4 summarizes the range of mean measured BAFs that were reported for four upper trophic level fish species (English Sole, Staghorn Scullpin, Whitespotted Greenling, and Spiny Dogfish) in a study of False Creek Harbor, Vancouver, Canada. Given an assumed reference lipid content of 5%, these values can be compared to the lipid normalized BAF criterion of 5,000/.05 = 100,000 or log BCF_{lipid} = 5.0. This comparison indicates that measured field BAFs for all but one substance (i.e. 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester or more commonly known as butyl benzyl phthalate) fall below the B criterion supporting EC's initial categorization of these substances as "Not B".

Table 4. Field-Derived BAFs for Phthalates in Four Upper Trophic Level Fish Species.

CAS #	Chemical Name	Predicted Log K_{ow}	Initial Assessment	Measured Fish BAF_{lipid} Log (l/kg lipid)
131113	1,2-Benzenedicarboxylic acid, dimethyl ester	1.66	Not B	3.96-4.28
84662	1,2-Benzenedicarboxylic acid, diethyl ester	2.65	Not B	2.95-3.71
84695	1,2-Benzenedicarboxylic acid, bis(2-methylpropyl) ester	4.46	Not B	3.49-4.45
84742	1,2-Benzenedicarboxylic acid, dibutyl ester	4.61	Not B	3.28-4.35
85687	1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester	4.84	EMP >5000	4.07-5.31
68515504	1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear	6.46	NA	3.39-3.67
71888896	1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters,C7-rich	7.41	NA	1.44-2.60
117817	1,2-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester	8.39	Not B	2.68-3.70
27554263	1,2-Benzenedicarboxylic acid, diisooctyl ester	8.39	>=1 BCF model	1.46-2.32
117840	1,2-Benzenedicarboxylic acid, dioctyl ester	8.54	Not B	2.57-2.95
28553120	1,2-Benzenedicarboxylic acid, diisononyl ester	9.37	1 BAF model	3.59
84764	1,2-Benzenedicarboxylic acid, dinonyl ester	9.52	Not B	2.64
68515480	1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich	9.52	NA	3.59
68515491	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich	10.28	NA	3.02-3.46
68515435	1,2-Benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters	10.39	NA	3.02-3.46

It is important to point out that the observed field BAFs for a number of the low molecular weight phthalates are much greater than would be expected based on Log K_{ow} considerations. One possible explanation for unexpectedly high BAFs is dis-equilibrium between overlying water and sediment porewater concentrations. If concentrations in sediment porewater are significantly higher than overlying water, concentrations in benthic prey, which are ingested by upper trophic level organisms, are much higher than would be expected if equilibrium is assumed. In such situations, field BAFs that are obtained by dividing upper trophic biota by overlying water concentrations do not provide the appropriate exposure normalization since bioaccumulation also depends on exposure mediated via sediment porewater. As a result field-derived BAFs can, in some cases, incorrectly exaggerate bioaccumulation potential and thus provide a misleading technical basis for B assessment.

Since sediment concentrations were also measured in this field study, it is possible to assess the extent of dis-equilibrium between these compartments for the various phthalates investigated. This was done by Mackintosh (2003) by comparing the observed organic-carbon normalized sediment-water partition coefficients (K_{oc}) derived from field measurements to K_{oc} values derived using equilibrium partitioning theory.[17] Resulting calculations are summarized in Table 5 and indicate significant dis-equilibrium between overlying and sediment compartments particularly for the lower molecular weight phthalates. Since all of the fish species in this study have a benthic prey component, the absolute magnitude of the field-derived BAF must be interpreted with caution and not used alone as the basis for B regulatory decision-making. A less ambiguous approach for analysis and interpretation of such field data is to plot lipid-normalized concentrations in all species of the foodweb as function of trophic position. Substances, such as selected PCB congeners, that exhibit a high bioaccumulation potential will exhibit a positive slope with trophic position. Linear regression analysis of lipid normalized concentrations of PCBs measured in this same field study confirmed a significant positive slope with trophic position. In contrast, lipid normalized phthalate concentrations did not significantly increase with trophic level. In fact, C4 to C7 phthalates (including benzyl butyl phthalate) exhibit a slight, but not statistically significant decline in concentrations whereas C8 and higher phthalates demonstrate a significant negative slope, providing clear evidence of trophic dilution.[18]

Table 5. Comparison of Field-Derived Organic Carbon Normalized Sediment-Water Partition Coefficients to Calculated Values using Equilibrium PartitioningTheory.

Phthalate	K_{oc} Ratio (Field Measured / Theory)
Di-methyl	17,700
Di-ethyl	28.9
Di-isobutyl	4.8
Di-n-butyl	6.0
Butyl benzyl	43.9
Di-2-ethylhexyl	28.6
Di-n-octyl	14.8
Di-n-nonyl	2.7
Di-isohexyl	2.7
Di-isoheptyl	11.6
Di-isoctyl	32.3
Di-isononyl	21.6
Di-isodecyl	19.8

To develop a further weight of evidence for B assessment, results from laboratory tests are compiled in Table 6. Measured fish bioconcentration factors for parent phthalates were obtained from the comprehensive literature review by Staples et al. (1997).[4] While data are limited, measured BCFs are below the EC BCF criterion over a wide range of Log K_{ow}. Moreover, measured BCFs are consistently below BCFwin QSAR model predictions. Two dietary bioaccumulation studies that include a number of individual phthalates are also available that enable experimental biomagnification factor (BMF) values (defined as the lipid-normalized concentration in fish to that in the diet at steady state) to be calculated and compared with default BMFs used in the Gobas BAF model. For phthalates and adipates with log K_{ow} in the range of 4 to 9, experimentally derived BMFs are orders of magnitude lower than BMFs calculated from default values, providing empirical evidence of extensive biotransformation in both the fish gut and tissue. Laboratory bioconcentration and dietary bioaccumulation test data for butyl benzyl phthalate, indicating a low inherent bioaccumulation potential, provide further compelling evidence that the field-derived BAF discussed previously does not provide an accurate characterization of the bioaccumulation potential of this substance.

Table 6. Laboratory Studies for Bioaccumulation Assessment of Phthalates and Adipates.

CAS #	Chemical Name	Predicted Log Kow	Predicted BCFwin log BCF	Measured Fish log BCF	Default Fish BMF (lipid basis)	Measured Fish BMF (lipid basis)	Reference
	Phthalates						
131113	1,2-Benzenedicarboxylic acid, dimethyl ester	1.66	0.532		0.0013	0.0003-0.0010	19
84662	1,2-Benzenedicarboxylic acid, diethyl ester	2.65	1.163		0.005	0.0012-0.0022	19
84742	1,2-Benzenedicarboxylic acid, dibutyl ester	4.61	2.765	2.22	0.35	0.0044-0.0102	4,19
85687	1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester	4.84	2.942	1.08	0.56	0.0013-0.0018	4,19
71888896	1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters,C7-rich	7.41	2.75		4.48	<0.002 - 0.027	20
117817	1,2-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester	8.39	2.488	2.45	1.21	<0.0026 - <0.008	19,20
117840	1,2-Benzenedicarboxylic acid, dioctyl ester	8.54	1.803		0.91	0.0002-0.0004	19
68515480	1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich	9.52	0.5		0.11	<0.0034	20
68515491	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich	10.28	0.5		0.019	<0.0049	20
	Adipates						
103231	Hexanedioic acid, bis(2-ethylhexyl) ester	8.12	2.56	1.43			21
151326	Hexanedioic acid, dinonyl ester	9.24	0.5		0.20	0.006	20
105975	Hexanedioic acid, didecyl ester	10.23	0.591		0.021	0.009	20

Based on the comparison of BCFwin QSAR model predictions to measured BCF data, this model is expected to provide a conservative basis for B assessment of phthalates and adipates for which there is currently no field or laboratory data. While no B data are available for trimellitates, the structural similarity with phthalates provides an appropriate basis for read across. Figure 4 provides a plot of BCFwin predictions for all 93 substances considered in this report as a function of Log K_{ow}. Four substances were found to have predicted BCF values obtained from this model that exceed the EC B criterion of 5,000:

- 1,2-Benzenedicarboxylic acid, dicyclohexyl ester (CAS # 84617)
- 1,2-Benzenedicarboxylic acid, isooctyl phenylmethyl ester (CAS # 27215221)
- 1,2-Benzenedicarboxylic acid, bis(methylcyclohexyl) ester (CAS # 27987253)
- 1,2-Benzenedicarboxylic acid, benzyl C7-9-branched & linear alkyl esters (CAS # 68515402)

In the absence of measured BAF or BCF data, these compounds can be tentatively identified as potentially bioaccumulative for DSL categorization.

The recommendation to not categorize any of the dialkyl phthalate esters or butyl benzyl phthalate ester as bioaccumulative is consistent with the U.S. Environmental Protection Agency's (USEPA) evaluation performed as part of the Great Lakes Water Quality Initiative. In this final rule, USEPA categorized dimethyl, diethyl, di-n-butyl, butyl benzyl, di-2-ethyl hexyl, and di-n-octyl phthalate as substances that were not bioaccumulative chemicals of concern (BCC).[22] BCCs were defined by the USEPA as "any chemical that has the potential to cause adverse effects which, upon entering the surface waters, by itself or as its toxic transformation product, accumulates in aquatic organisms by a human health bioaccumulation factor greater than 1000, after considering metabolism and other physiochemical properties that might enhance or inhibit bioaccumulation".

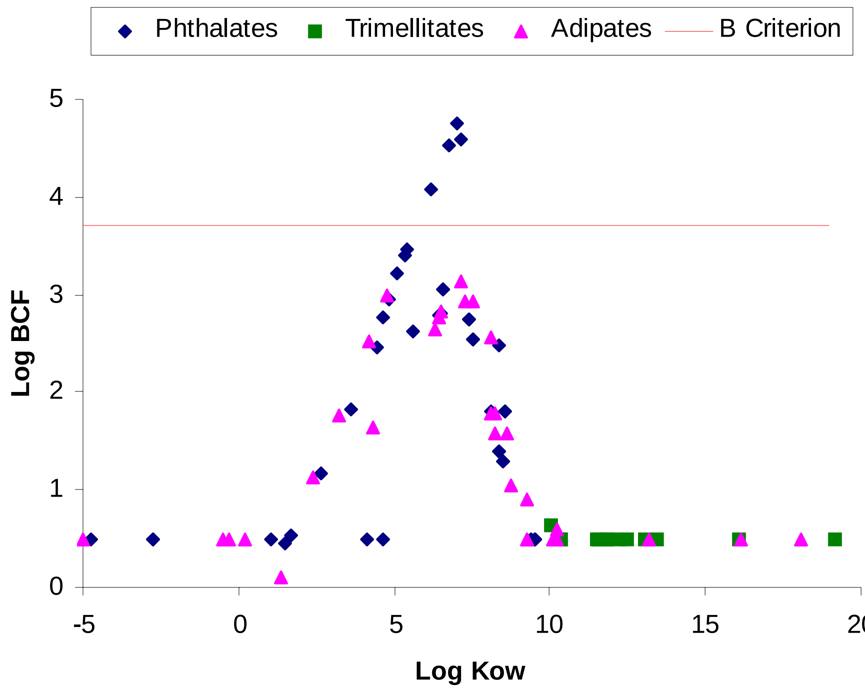

Figure 4. BCFwin Predictions as a Function of Log K_{ow} for all 93 Substances Evaluated in This Report.

VI. Aquatic Toxicity Assessment

A search for aquatic toxicity data was conducted for the 93 phthalates, trimellitates, adipates, and related monoesters addressed in this report (Appendix 1). Available data are largely from the public literature[23,24,25,26,27,28,29], but also include a company report.[30] These data together with log K_{ow} values obtained from EPIWIN were used as the basis for iT characterization of the 93 substances.

The criteria for iT characterization used by EC are <1.0 and <0.1 mg/L for acute and chronic toxicity, respectively. A provisional iT assessment was performed by EC for 41 of the substances. The remaining 52 substances were either "not assessed" or identified as "uncertain" by EC. Of the 41 substances assessed by EC, 21 were initially characterized as "iT". They included 14 phthalates, evaluated through the application of QSAR (Quantitative Structure-Activity Relationship) modeling or experimental data, 6 adipates, evaluated through QSAR modeling, and 1 monoester through experimental data. No trimellitates were initially classified as iT.

To the extent possible, substances were evaluated either with data developed specifically for that substance or, where justifiable, with data using read-across principles. Acute and chronic values for selected substances were listed as above or below the respective EC criterion (i.e., >1 mg/L or <1 mg/L). The read-across strategy involved associating measured data for a substance to a similar substance without data to predict that endpoint for the substance without data. Two general read-across principles that were applied were:

- Chemical relatedness - the substance without data as well as the substance(s) with data must be similar such that their physicochemical, biological, and toxicological properties would be expected to behave in a predictably similar manner or logically progress within a defined range.
- Structural similarity - the substance without data must possesses small incremental structural differences from the reference substance(s) or the difference between the two must not affect the property to the extent that it cannot be accurately predicted.

For the substances under consideration, in general, read-across can be applied across increasing/decreasing carbon (C) numbers in the side-chains. For example, data for a dinonyl (di-C9) phthalate and diundecyl (di-C11) phthalate can be used to read-across to a didecyl (di-C10) phthalate or a phthalate diester with constituents that contain a range of C9 to C11 alkyl groups.

Data were found that could be applied either specifically or as read-across for 46 of the 93 substances in this evaluation. Table 7 summarizes the Log K_{ow} values and iT conclusions for the substances for these substances. Further analysis of Table 7 reveals substances with log K_{ow} values less than approximately 4.5 that are not characterized as "iT" because their acute and/or chronic effect concentrations(s) fall above the respective criterion. In contrast, substances falling within a log K_{ow} range of approximately 4.5 to 6.5 can be considered iT. Where data are available to characterize substances within this log K_{ow} range, either the acute and/or chronic effect concentration(s) falls below the respective EC criterion. (note: ">WS" indicates that no toxicity was observed at the maximum water solubility of the test material).

Characterization of selected higher molecular weight substances as "Not iT" beginning with the two di-C6 alkyl phthalates, which have log K_{ow} values of approximately 6.5, is consistent with the conclusions reached in previous aquatic toxicity literature reviews for phthalates.[29,31] Data summarized in these reviews and assessed as reliable show that no measurable acute and chronic effects are reported for phthalates with molecular weights equal to or greater than a di-C6 alkyl phthalate. The two di-C6 alkyl phthalates are 1,2-benzenedicarboxylic acid, dihexyl ester (log K_{ow} = 6.57) and 1,2-benzene-dicarboxylic acid, dihexyl ester, branched and linear (log K_{ow} = 6.46). These substances either do not or would not be expected to exhibit acute or chronic toxicity at their water solubility limit. The water solubility of a di-C6 alkyl phthalate containing branched C6 mixed isomers, has been reported as 0.07 mg/L at 22°C.[32]

Table 7. Summary of Aquatic Toxicity Test Data / Read-Across Assessments for Selected Phthalates, Adipates and Trimellitates. Toxicity Results are Indicated as Above or Below Acute (1 mg/L) and/or Chronic (0.1 mg/L) Criteria. For Comparison, Initial iT Proposals by EC are Listed Next to Recommended iT Positions Obtained from Analysis of Measured Data.

Chemical Name	Predicted Log K_{ow} (a)	Measured Acute Toxicity	Measured Chronic Toxicity	Initial EC iT Assessment	Recommended iT Assessment
Hexanedioic acid	0.23	>1mg/L (b)	nd	Not iT (Exp)	Not iT (Exp)
1,2-Benzenedicarboxylic acid, dimethyl ester	1.66	>1mg/L (c)	>0.1mg/L (c)	Not iT (Exp)	Not iT (Exp)
Hexanedioic acid, diethyl ester	2.37	>1mg/L (d)	nd	Not iT (Exp)	Not iT (Exp)
1,2-Benzenedicarboxylic acid, diethyl ester	2.65	>1mg/L (c)	>0.1mg/L (c)	Not iT (Exp)	Not iT (Exp)
Hexanedioic acid, dibutyl ester	4.33	>1mg/L (e)	nd	Not iT (Exp)	Not iT (Exp)
1,2-Benzenedicarboxylic acid, bis(2-methylpropyl) ester	4.46	<1mg/L (c)	nd	IT (Exp)	iT (Exp)
1,2-Benzenedicarboxylic acid, dibutyl ester	4.61	<1mg/L (c)	≥0.1mg/L (c)	IT (Exp)	iT (Exp)
1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester	4.84	<1mg/L (c)	<0.1mg/L (c)	IT (Exp)	iT (Exp)
1,2-Benzenedicarboxylic acid, butyl 2-ethylhexyl ester	6.50	>WS (c)	<0.1mg/L (c)	IT (QSAR)	iT (Exp)
1,2-Benzenedicarboxylic acid, dihexyl ester, branched and linear	6.46	>WS (c)	>0.1mg/L (c)	Not Assessed	Not iT (RA)
1,2-Benzenedicarboxylic acid, dihexyl ester	6.57	>WS (c)	>0.1mg/L (c)	IT (QSAR)	Not iT (Exp)
1,2-Benzenedicarboxylic acid, benzyl C7-9-branched and linear alkyl esters	7.15	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters, C7-rich	7.41	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
1,2-Benzenedicarboxylic acid, diheptyl ester, branched and linear	7.41	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
Hexanedioic acid, di-C7-9-branched and linear alkyl esters	7.55	>WS (g)	nd	Not Assessed	Not iT (Exp/RA)

Table 7. (continued)

Chemical Name	Predicted Log K_{ow} (a)	Measured Acute Toxicity	Measured Chronic Toxicity	Initial iT Assessment	Recommended IT Assessment
1,2-Benzenedicarboxylic acid, di-C7-11-alkyl esters	7.56	>WS (c)	nd	Not Assessed	Not iT (Exp/RA)
1,2-Benzenedicarboxylic acid, mixed decyl and hexyl and octyl diesters	8.10	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
Hexanedioic acid, bis(2-ethylhexyl) ester	8.12	>WS (g)	>WS (g)	Uncertain	Not iT (Exp)
Hexanedioic acid, bis(2-ethylhexyl) ester	8.12	>WS (g)	>WS (g)	Uncertain	Not iT (Exp)
1,2-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester	8.39	>WS (c)	>WS (f)	IT (Exp)	Not iT (Exp)
1,2-Benzenedicarboxylic acid, diisooctyl ester	8.39	>WS (c)	nd	IT (QSAR)	Not iT (Exp/RA)
1,2-Benzenedicarboxylic acid, heptyl nonyl ester, branched and linear	8.39	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
1,2-Benzenedicarboxylic acid, di-C7-11-branched and linear alkyl esters	8.47	>WS (c)	nd	Not Assessed	Not iT (Exp/RA)
1,2-Benzenedicarboxylic acid, di-C7-9-branched and linear alkyl esters	8.47	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
1,2-Benzenedicarboxylic acid, dioctyl ester	8.54	>WS (c)	>WS (c)	IT (QSAR)	Not iT (Exp)
1,2-Benzenedicarboxylic acid, decyl hexyl ester	8.54	>WS (c)	>WS (f)	Uncertain	Not iT (Exp)
Hexanedioic acid, di-C7-9-alkyl esters	8.75	>WS (g)	nd	Not Assessed	Not iT (Exp/RA)
Hexanedioic acid, diisononyl ester	9.24	>WS (h)	nd	Uncertain	Not iT (Exp/RA)
Hexanedioic acid, dinonyl ester	9.24	>WS (h)	nd	Uncertain	Not iT (Exp/RA)
1,2-Benzenedicarboxylic acid, diisononyl ester	9.37	>WS (c)	>WS (f)	IT (QSAR)	Not iT (Exp)
1,2-Benzenedicarboxylic acid, heptyl undecyl ester, branched and linear	9.37	>WS (c)	nd	Not Assessed	Not iT (Exp/RA)
1,2-Benzenedicarboxylic acid, dinonyl ester	9.52	nd	>WS (f)	Uncertain	Not iT (RA/Exp)
1,2-Benzenedicarboxylic acid, decyl octyl ester	9.52	nd	>WS (f)	Uncertain	Not iT (RA/Exp)

Table 7. (continued)

Chemical Name	Predicted Log K_{ow} (a)	Measured Acute Toxicity	Measured Chronic Toxicity	Initial iT Assessment	Recommended IT Assessment
1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich	9.52	>WS (c)	>WS (f)	Not Assessed	Not iT (Exp)
1,2-Benzenedicarboxylic acid, dinonyl ester, branched and linear	9.52	>WS (c)	>WS (f)	Not Assessed	Not iT (Exp)
1,2-Benzenedicarboxylic acid, mixed decyl and octyl diesters	9.52	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich	10.28	>WS (c)	>WS (f)	Not Assessed	Not iT (Exp)
1,2-Benzenedicarboxylic acid, nonyl undecyl ester, branched and linear	10.28	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
1,2-Benzenedicarboxylic acid, diisodecyl ester	10.36	>WS (c)	>WS (f)	Not Assessed	Not iT (Exp)
1,2-Benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters	10.39	nd	>WS (f)	Not Assessed	Not iT (RA/Exp)
1,2-Benzenedicarboxylic acid, diundecyl ester	11.49	>WS (c)	>WS (f)	Not Assessed	Not iT (Exp)
1,2,4-Benzenetricarboxylic acid, tris(2-ethylhexyl) ester	11.59	>WS (h)	nd	Not iT (Exp)	Not iT (Exp/RA)
1,2-Benzenedicarboxylic acid, diundecyl ester, branched and linear	11.83	>WS (c)	>WS (f)	Not Assessed	Not iT (Exp)
1,2-Benzenedicarboxylic acid, di-C11-14-branched alkyl esters, C13-rich	12.25	>WS (c)	>WS (f)	Not Assessed	Not iT (Exp)
Hexanedioic acid, ditridecyl ester	13.17	>WS (g)	nd	Uncertain	Not iT (Exp/RA)
1,2-Benzenedicarboxylic acid, ditridecyl ester	13.45	>WS (c)	>WS (f)	Not Assessed	Not iT (Exp)

a EPIWIN, 1999; b Mattson et al., 1976; c Staples et al., 1997

d Brooke et al., 1984; e Geiger et al., 1985; f Brown et al., 1998

g Aliphatic Esters Panel of the American Chemistry Council, 2003

h EBSI, 1996; i Phthalate Esters Panel of the American Chemistry Council, 2001

nd - no data; WS - water solubility; Exp - from experimental data; RA - from read-across data

QSAR – Quantitative Structure-Activity Relationship

To assess iT for the remaining 47 substances for which measured data are not directly applicable, the observed toxicity-log K_{ow} relationship obtained from analysis of Table 7 discussed above was applied. Thus, in the absence of relevant measured data, substances with log K_{ow} in the range of 4.5 to 6.5 are provisionally categorized as "iT" while substances that fall below or above this range are considered "Not iT". Table 8 lists the 15 substances which likely meet EC's iT criteria based on available measured toxicity data or lacking such information, analogy using log K_{ow}.. Of the 15 substances, 4 have been associated with acute and/or chronic data that allow characterization based on experimental data. Also within this group, EC initially characterized 3 of these substances as "Not iT". For the remaining substances, the recommendations provided in Table 8 agree with the EC findings that iT criteria are met.

1,2-Benzenedicarboxylic acid, butyl 2-ethylhexyl ester (log K_{ow} = 6.50) is the highest log K_{ow} substance, with chronic data that fall below the iT criterion (Table 7). The two exceptions in Table 8 with log K_{ow} values slightly greater than 6.5 that do not have substances-specific measured data, but are also provisionally considered "iT" are 1,2-benzenedicarboxylic acid, butyl octyl ester (log K_{ow} = 6.57) and hexanedioic acid, octyl phenylmethyl ester (log K_{ow} = 6.53). The former is conservatively designated as "iT" because of its structural similarity to 1,2-benzenedicarboxylic acid, butyl 2-ethylhexyl ester. In this case, the chronic toxicity data for 1,2-benzenedicarboxylic acid, butyl 2-ethylhexyl ester are used as read-across to 1,2-benzenedicarboxylic acid, butyl octyl ester. In comparison, hexanedioic acid, octyl phenylmethyl ester is potentially considered as "iT" because there are insufficient measured ecotoxicity data on benzyl adipates beyond the QSAR used by EC to justify an alternative view.

EC in its review of data used to initially characterize iT, incorrectly represented 3 data points used in its evaluation and also relied on 1 data point that is questionable when considered against the weight of evidence for that substance. Those data and the correct values or the rationale for exclusion are:

- The iT characterization for 1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester was based on an algal 96-hour EC_{50} value that was incorrectly cited as 0.1 mg/L. The correct value is >0.1 mg/L (>WS), i.e., it did not produce acute effects at the maximum concentration tested which exceeds the aqueous solubility of this substance by almost two orders of magnitude.[32]
- The iT characterization for 1,2-benzenedicarboxylic acid, dihexyl ester was based on a fish 96-hour LC_{50} value that was incorrectly cited as 0.1 mg/L. The correct value is >0.1 mg/L (>WS), i.e., indicating that it did not produce acute effects at the maximum concentration tested which exceeds the aqueous solubility of this substance by more than an order of magnitude.[32]
- The iT characterization for 1,2-benzenedicarboxylic acid, butyl 2-ethylhexyl ester is probably accurate. However, it is based on an invertebrate 48-hour EC_{50} value that is incorrectly cited as 0.07 mg/L. The correct value is >0.07 mg/L (>WS), which indicates that it did not produce acute effects at the limit of solubility as measured under the test conditions. However available chronic data for daphnia indicate a NOEC that is that below the water solubility for this substance and also just below the EC chronic criterion of 0.1 mg/l. Therefore, available chronic data justify iT categorization.[29,32]
- The iT characterization for 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester is also deemed accurate. However, it is based on an oyster 48-hour EC_{50} value reported as 0.017 mg/L. This value is approximately 1 to 2-orders of magnitude lower than all other acute results (Staples *et al*., 1997), which fall between approximately 0.1 to 4 mg/L.

Table 8. Phthalates, Adipates and Trimellitates on the DSL that Meet (Measured Data) or Likely Meet (by Analogy) iT Criteria. Toxicity Data are represented as either Above or Below Acute (1 mg/L) and/or Chronic (0.1 mg/L) Criteria. For Comparison, Initial iT Proposals by EC are Listed Next to Recommended iT Positions Obtained From Analysis of Measured Data.

Chemical Name	Predicted Log K_{ow} (a)	Measured Acute Toxicity	Measured Chronic Toxicity	Initial iT Assessment	Recommended iT Assessment
1,2-Benzenedicarboxylic acid, bis(2-methylpropyl) ester	4.46	<1mg/L (c)	nd	iT (Exp)	iT (Exp/RA)
1,2-Benzenedicarboxylic acid, dibutyl ester	4.61	<1mg/L (c)	≥0.1mg/L (c)	iT (Exp)	iT (Exp)
1,2,4-Benzenetricarboxylic acid, isooctyl ester*	4.61	nd	nd	Not Assessed	iT (RA)
Hexanedioic acid, bis(phenylmethyl) ester	4.8	nd	nd	iT (QSAR)	iT (RA)
1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester	4.84	<1mg/L (c)	<0.1mg/L (c)	iT (Exp)	iT (Exp)
1,2-Benzenedicarboxylic acid, bis(phenylmethyl) ester	5.08	nd	nd	iT (QSAR)	iT (RA)
1,2-Benzenedicarboxylic acid, cyclohexyl 2-methylpropyl ester	5.33	nd	nd	Not iT (QSAR)	iT (RA)
1,2-Benzenedicarboxylic acid, butyl cyclohexyl ester	5.41	nd	nd	Not iT (QSAR)	iT (RA)
1,2-Benzenedicarboxylic acid, dipentyl ester	5.59	nd	nd	iT (QSAR)	iT (RA)
1,2-Benzenedicarboxylic acid, dicyclohexyl ester	6.20	nd	nd	Not iT (QSAR)	iT (RA)
Hexanedioic acid, dihexyl ester	6.30	nd	nd	iT (QSAR)	iT (RA)
Hexanedioic acid, 2-ethylhexyl phenylmethyl ester	6.46	nd	nd	iT (QSAR)	iT (RA)
1,2-Benzenedicarboxylic acid, butyl 2-ethylhexyl ester	6.50	>WS (c)	<0.1mg/L (c)	iT (QSAR)	iT (Exp)
Hexanedioic acid, octyl phenylmethyl ester	6.53	nd	nd	iT (QSAR)	iT (RA)
1,2-Benzenedicarboxylic acid, butyl octyl ester	6.57	nd	nd	iT (QSAR)	iT (RA)

a EPIWIN, 1999; b Geiger *et al*., 1985; c Staples *et al*., 1997

* Substance is a trimellitate monoester and read across is applied to the un-ionized form. This assumption is likely conservative since a significant fraction is likely to be in the less toxic, ionized form at normal pH of receiving water.

nd - no data; Exp - from experimental data; RA - from read-across data; WS - water solubility

QSAR – Quantitative Structure-Activity Relationship

For the remaining 78 substances not included in Table 8, measured toxicity data or read-across principles support a "Not iT" designation.

VII. Conclusions

A comprehensive review of persistence, bioaccumulation, and aquatic toxicity data was conducted for 93 selected phthalates, trimellitates, adipates, and related monoesters on the DSL to support PBiT categorization using criteria established by EC. Considerable information was available to provide recommended P, B, and iT categorization for all substances evaluated in this study.

The following 3 substances were modeled as meeting the criteria for P:

- 1,2-Benzenedicarboxylic acid, dimethyl ester (CAS# 131113)
- 1,2-Benzenedicarboxylic acid, diethyl ester (CAS# 84662)
- Hexanedioic acid, dimethyl ester (CAS# 627930)

The following 4 substances were modeled as meeting the criteria for B:

- 1,2-Benzenedicarboxylic acid, dicyclohexyl ester (CAS# 84617)
- 1,2-Benzenedicarboxylic acid, isooctyl phenylmethyl ester (CAS# 27215221)
- 1,2-Benzenedicarboxylic acid, bis(methylcyclohexyl) ester (CAS# 27987253)
- 1,2-Benzenedicarboxylic acid, benzyl C7-9-branched & linear alkyl esters (CAS# 68515402)

The following 15 substances were identified by data or read-across as meeting the criteria for iT:

- 1,2-Benzenedicarboxylic acid, bis(2-methylpropyl) ester (CAS# 84695)
- 1,2-Benzenedicarboxylic acid, dibutyl ester (CAS# 84742)
- 1,2,4-Benzenetricarboxylic acid, isooctyl ester (CAS# 68186323)
- 1,2-Benzenedicarboxylic acid, butyl phenylmethyl ester (CAS# 85687)
- 1,2-Benzenedicarboxylic acid, bis(phenylmethyl) ester (CAS# 523319)
- 1,2-Benzenedicarboxylic acid, cyclohexyl 2-methylpropyl ester (CAS# 5334098)
- 1,2-Benzenedicarboxylic acid, butyl cyclohexyl ester (CAS# 84640)
- 1,2-Benzenedicarboxylic acid, dipentyl ester (CAS# 131180)
- 1,2-Benzenedicarboxylic acid, dicyclohexyl ester (CAS# 84617)
- 1,2-Benzenedicarboxylic acid, butyl 2-ethylhexyl ester (CAS# 68515504)
- 1,2-Benzenedicarboxylic acid, butyl octyl ester (CAS# 84786)
- Hexanedioic acid, dihexyl ester (CAS# 110338)
- Hexanedioic acid, bis(phenylmethyl) ester (CAS# 2451845)
- Hexanedioic acid, octyl phenylmethyl ester (CAS# 3089552)
- Hexanedioic acid, 2-ethylhexyl phenylmethyl ester (CAS# 58394642)

Only one substance, *1,2-benzenedicarboxylic acid, dicyclohexyl ester* (CAS# 84617), was identified as potentially meeting the EC criteria for BiT. No substances were identified as meeting criteria for PiT or PBiT.

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Rationale for Removing Diisodecyl Phthalate Ester (DIDP; CAS #68515-49-1) from the Washington State Department of Ecology PBT List

ExxonMobil Biomedical Sciences, Inc.

The Washington State Department of Ecology (Ecology) evaluated selected phthalate esters for possible inclusion on a PBT list. Di-isodecyl phthalate (DIDP), CAS #68515-49-1, was determined to meet persistence and bioaccumulation criteria specified in WAC 173-333-320. However, the identification of DIDP as persistent and bioaccumulative is based on an incorrect structure (SMILES) and overly conservative assumptions, and the evaluation does not take into consideration measured data that show DIDP is readily biodegradable and therefore not persistent. The conclusion that DIDP is bioaccumulative is also incorrect because it relies on data that cannot be correlated to parent test material and with a test species that is not traditionally used to evaluate this endpoint. Additionally, this evaluation does not take into consideration recently published data that show DIDP does not biomagnify through a food-web, but rather shows evidence of decreasing in concentration from lower to higher trophic levels.

Data are provided below that support characterizing DIDP as not persistent and not bioaccumulative. This information is briefly summarized at this time and will be further elaborated on in a formal reply to Ecology to be submitted in November 2005.

Persistence

The data used to include DIDP, CAS #68515-49-1, on the list for persistence are based on computer modeled information that were developed using the U.S. Environmental Protection Agency (EPA) PBT Profiler, which calculates media-specific half-life values based on CAS number and structure. Additional half-life values in various media are also cited by Ecology and taken from the European Chemicals Bureau.

The structure identified by the PBT Profiler model with the use of CAS #68515-49-1 contains a quaternary carbon-branched structure in each of the two alkyl groups in the phthalate ester molecule. However, the alkyl groups in DIDP represent a mixture of various isomers that is not representative of this unique structure type. The alkyl groups in DIDP are branched, but the branching is present along the alkyl chain as primarily methyl groups. Structure-based computer models are trained to recognize quaternary carbon structures as persistent, which is why the Profiler model identified the CAS number associated with DIDP as having long media half-life values.

The European Chemicals Bureau (ECB, 2003) estimated half-life values for DIDP using overly conservative assumptions. In their assessment, ECB calculates half-life based on freely dissolved material. DIDP has a very low water solubility, less than 1 ppb. As such, this directly impacts the biodegradation rate, resulting in unrealistically longer half-life values.

Ecology did not consider in their evaluation biodegradation data, which shows that DIDP biodegraded to 67% after 28 days and was readily biodegradable (Exxon, 1995). This study was conducted following the OECD 301F, Manometric Respirometry Biodegradation Test guideline. Using Robert Boethling's (U.S. EPA) extrapolation approach (Environment Canada, 2003) the biodegradation rate constant, water, soil, and sediment half-life values are 0.1400 (k)(day^{-1}), 5 days, 5 days, and 20 days, respectively. These half-life values are clearly below the criteria used by Ecology to identify persistent substances. Additionally, Environment Canada has determined that DIDP is not persistent based on information supplied by ExxonMobil Biomedical Sciences, Inc. (2004).

Bioaccumulation

The data used to include DIDP, CAS #68515-49-1, on the list for bioaccumulation are based on the results of a study that uses total radioactivity to measure bioconcentration. In its document, Ecology states that the information it identifies comes from a report (ECB, 2003) which states:

> The use of BCF values based on total radioactivity may give an overestimation of the BCF due to the fact that the metabolism of DIDP was not taken into account as both ^{14}C-DIDP and any ^{14}C-labeled metabolites of DIDP were measured (including ^{14}C built into the tissue of the organism in e.g. fatty acids).

Although Ecology suggests that these data may underestimate potential bioaccumulation, the fact remains that bioaccumulation study designs using radiolabeled test material are no longer favored for regulatory decision making, especially when results exist that are based on measured parent test material. In its evaluation, Ecology may not have had the knowledge of recent data that show DIDP and similar high molecular weight phthalate esters do not bioaccumulate.

A field study evaluated the biomagnification of selected high molecular weight phthalate esters that included diisononyl and diisodecyl phthalate esters, through eighteen marine species representing several trophic levels (Mackintosh *et al*., 2004). Organisms evaluated by Mackintosh *et al*. (2004) included three primary producers (e.g., plankton and macroalgae), two filter feeders (mussel and oyster), two deposit feeders (clams), a crab, a starfish, eight fish species, and one sea duck. The authors concluded that the phthalate esters in their study do not biomagnify through the food-web, but rather decrease in tissue concentration with increasing trophic position. Decreasing concentrations can be quantified by food-web magnification factors (FWMFs). A FWMF that is greater than 1.0 is an indication of chemical biomagnification within a food web, whereas a value of less than 1.0 indicates trophic dilution, i.e., decreasing concentrations from lower to higher trophic levels. Mackintosh *et al*. (2004) showed that lipid equivalent concentrations of the high molecular weight phthalate esters, including diisononyl and diisodecyl phthalate esters, significantly declined with increasing trophic level.

In a related article that also presents results from the Mackintosh study (Gobas *et al.*, 2003), the authors describe food-web biomagnification under field conditions as bioaccumulation by predator and prey organisms that occurs through exposure to a chemical in both the aqueous habitat and diet. Thus, food-web bioaccumulation occurs when a lipid normalized chemical concentration increases in organisms with increasing trophic level, to the top predator. Gobas *et al.* (2003) concluded that high molecular weight phthalate esters do not biomagnify but rather show evidence of decreasing concentrations from lower to higher trophic levels which indicated that metabolic transformation is a key mitigating factor. The authors also mentioned that this lack of bioaccumulation is consistent with laboratory study and modeling results.

Bioconcentration factor (BCF) modeling, using the BCFWIN subroutine in the U.S. EPA EPI Suite model (2000), provides a BCF value of 3.2 for both di-nonyl phthalate ester (DINP) (CAS #68515-45-7) and di-decyl phthalate ester (CAS #68515-45-7).

These data support the conclusion that DINP and DIDP are not bioaccumulative chemicals of concern consistent with the recent PBT evaluation of these substances by Environment Canada.

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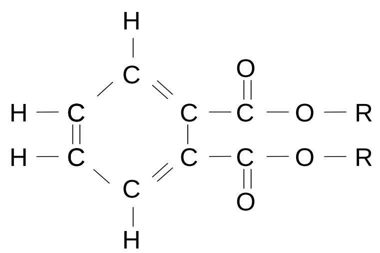
SIDS INITIAL ASSESSMENT PROFILE

Chemical Category	High Molecular Weight Phthalate Esters (HMWPE)	
Category Member CAS Registry Numbers and Chemical Names	53306-54-0	1,2-benzenedicarboxylic acid, di-2-propylheptyl ester
	68515-41-3	1,2-benzenedicarboxylic acid, di-C7-9-branched and linear alkyl esters
	85507-79-5	1,2-benzenedicarboxylic acid, di-C11-branched and linear alkyl esters
	68515-43-5	1,2-benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters
	3648-20-2	1,2-benzenedicarboxylic acid, di-C11-alkyl ester
	68515-47-9	1,2-benzenedicarboxylic acid, di-C11-14-branched alkyl esters, C13 rich
	119-06-2	1,2-benzenedicarboxylic acid, di-C13-alkyl ester
Category Member Structural Formulas	Substances in the High Molecular Weight Phthalate Esters Category have the following basic structure with alkyl groups (R) as indicated for the CAS registry numbers (RNs) below: 	
	53306-54-0	R=C10H21 (propyl branched) [100% branched]
	68515-41-3	R=C7H15 to C9H19 (branched and linear) [>80% linear]
	85507-79-5	R=C11H23 (branched, essentially methyl, and linear)
	68515-43-5	R=C9H19 to C11H23 (branched and linear) [>80% linear]
	3648-20-2	R=C11H23 (branched)
	68515-47-9	R=C13H27 (branched, essentially methyl)
	119-06-2	R=C13H27 (branched)

SUMMARY CONCLUSIONS OF THE SIAR

Category Justification

The High Molecular Weight Phthalate Ester (HMWPE) Category consists of esters with an alkyl carbon backbone with 7 carbon (C) atoms or greater. The category is formed on the principle that substances of similar structure have similar environmental and toxicological properties. Data are available on substances that meet the category definition and which are, or are not members of the category, to demonstrate that the members of this category have similar biological activities and that, when used, read-across is an appropriate approach to characterize endpoints for select members of this category.

The HMWPE Category contains chemically similar substances, 1,2-benzenedicarboxylic acid reacted with branched and/or linear alkyl alcohols, which are referred to as the alkyl chains in the phthalate ester molecule. A phthalate ester (PE) molecule is produced by esterifying one molecule of benzenedicarboxylic acid (phthalic anhydride) with two alcohol molecules. The seven members of this category contain linear and/or branched diheptyl, dioctyl, dinonyl, didecyl, diundecyl, didodecyl, and/or ditridecyl PEs. The branched alkyl chains are composed of varying mixed isomers. The length of the alkyl chains varies by substance, but the total carbon number of the longest linear C-chain (or backbone chain) is predominantly C7 or greater. For the seven substances in the category described in this submission, the backbones range from C7 to C12. The backbones in all but one category member contain methyl branching, only the bis-propyl heptyl phthalate backbone contains propyl branching.

Due to similar chemical structure, category members are generally similar with respect to select physico-chemical properties or display an expected trend (see Table 1 in SIAR). From the available data, HMWPE members are also similar with respect to their biological activity in that they demonstrate few biological effects.

For PEs, the critical toxicological effects are development and reproduction. These aspects are very structure dependent, and are associated with molecules with a 4 to 6 carbon backbone. By contrast, PEs with 7 or more backbone carbons produce no detectable effects in reproduction and no adverse effects on development. From a very large toxicology database for phthalate esters, a structure activity can be demonstrated that best relates to the linear portion of the phthalate ester, rather than total carbon number. For example, DINP (di-isononyl phthalate ester) and DIDP (di-isodecyl phthalate ester), are not formally part of this category as they have been assessed previously, but satisfy the category definition (as in Table 2 of the SIAR). Furthermore, for environmental effects, PEs do not show any effects from C5 upwards (see reference in SIAR). Hence, the HMWPE Category is valid for both toxicological and environmental endpoints.

As mentioned, DINP and DIDP, meet the category definition in that their backbone lengths are predominantly C7 or above, and produce little, if any, effects of developmental or reproductive toxicity. The DINP and DIDP dossiers have not been included in detail in this category, as they have already been assessed in the OECD HPV program:

- Di-isononyl phthalate ester (DINP); CAS RN 68515-48-0 and 28553-12-0
- Di-isodecyl phthalate ester (DIDP); CAS RN 68515-49-1 and 26761-40-0

However select data for these two substances will be used as supportive data to the category.

To correctly characterize selected endpoints for PEs, read-across techniques can be applied. Read-across is typically performed using measured or calculated data for an endpoint of interest for one or more like-substances to predict that endpoint for a similar substance without data.

Two general rules for read-across as they apply to PEs include:

- Chemical relatedness - the substance without data as well as the substance(s) with data are similar such that their physicochemical, biological, and toxicological properties would be expected to behave in a predictably similar manner or logically progress across a defined range. It is shown that for the environment assessment, read-across can be performed with HMWPE having a backbone chain length longer than 5 carbons. Indeed, since their water solubility is so low, there is no toxicity in fish, invertebrates, and algae for the HMWPE members at their limit of solubility. Read-across for the health assessment is performed with HMWPE having a backbone chain length of 7 carbons or greater.
- Structural similarity - the substance without data possesses small incremental structural differences from the reference substance(s) or the difference between the two will not affect the property sufficiently that it cannot be accurately predicted.

For PEs in general, read-across can be applied across increasing/decreasing carbon (C) numbers in the alkyl side-chains. For example, data for dinonyl (di-C9) phthalate and a diundecyl (di-C11) phthalate might be used to read-across to a didecyl (di-C10) phthalate or a phthalate diester with constituents that contain combinations of C9 to C11 alkyl groups. For purposes of discussion, the following general abbreviations will be used in this document to refer to PE members of this category:

- Di-phC10 PE (CAS RN 53306-54-0)
- Di-C7-9 PE (CAS RN 68515-41-3)
- Di-C11 PE (CAS RN 3648-20-2 or 85507-79-5)
- Di-C9-11 PE (CAS RN 68515-43-5)
- Di-C13 PE (CAS RN 68515-47-9 or 119-06-2)

Human Health

Data are not specifically available on the toxicokinetics, metabolism, or distribution of the HMWPE covered under this category. However, data developed for DINP are considered to be representative, in a qualitative point of view, of other HMWPE. When orally administered to rodents, DINP is rapidly metabolized in the gastrointestinal tract to the corresponding monoester (MINP), absorbed and excreted, primarily in the urine. Shortly after administration, it is found primarily in liver and kidneys, but it does not persist or accumulate in any organ or tissue. It is very poorly absorbed from the skin, but once absorbed it behaves in the same way as the orally administered substance. The results of these rodent studies contrast with data from studies involving humans or other primates, which indicate low absorption at low oral doses and even more limited total absorption at high doses. Indeed primates appear to be less efficient at metabolizing phthalates to the corresponding monoester, and at high doses absorption of monoester by primates is saturated. One reason for this difference is that there are differing hydrolysis rates for the phthalates between primates and rodents. Consequently, less HMWPE is likely to be absorbed in humans than in rodents.

HMWPE have a low order of acute toxicity by the inhalation, dermal, intraperitoneal and oral routes of exposure. Members of the HMWPE Category are not irritating to the skin or eyes (only slight conjunctival irritation for CAS RN 68515-47-9), neither are they skin sensitizers (Maximization Test or comparable, or Buehler Method). Although some data for these endpoints are older and the peer reviewed publications may not include all desirable methodology, the weight of evidence is consistent.

The primary findings in the repeated dose rat studies were in the liver and kidney and to a lesser degree in the thyroid. Effects to the liver, besides some minor and probably adaptative effects, are indicative of peroxisomal proliferation, including increased PCoA, liver weights, and liver hypertrophy and are not relevant for humans. Indeed, it has been shown that these effects are mediated through the peroxisome proliferation-activated receptor alpha (PPARα) and that levels of PPARα are much higher in rodents than humans. Thus, one would expect humans to be substantially less responsive than rodents to peroxisome proliferating agents. Empirical evidence for this hypothesis has been provided by studies in primates in which repeated administration of DINP had no effects on liver, kidney or testicular parameters, including peroxisome proliferation. The kidney effects were a result of a dose-dependent α-2μ-globulin nephropathy. Such effects are sex- and species-specific to male rats and also are not relevant to humans. The relevance of sporadically observed increased kidney weights in female rats is unclear. Thyroid effects are likely to be a compensatory effect associated with the peroxisomal proliferation in the liver. The results were consistent for all members of the Category, with NOAEL ranging between 10 and 282 mg/kg/day. It should be noted that the 10 mg/kg/day value comes from an OECD 422 study, where rats were dosed for 45 days and the effect observed at 50 mg/kg/day was liver weight increase. This is likely to be related to peroxisome proliferation. The spread in this data is driven by the dose level selection in the various tests. All the NOAELs are driven by liver and/or kidney (common) effects.

HMWPE Category members have been tested in the Ames reverse mutation assay using *Salmonella typhimurium* and all were non-mutagenic with and without metabolic activation. Similarly, a range of substances covering the majority of the carbon numbers in this category were found to be inactive in the mouse lymphoma tests. Additional testing of di-C13 PE showed that the test substance did not induce either structural chromosomal aberrations or polyploidy in CHL cells up to the limit concentration of 4.75 mg/ml, in the absence or presence of an exogenous metabolic activation system. These substances are non-genotoxic based on the negative genotoxicity data for the category as a whole. Although some data for these endpoints are older and the peer reviewed publications may not include all desirable methodology, the weight of evidence is consistent.

Although the HMWPE have not been tested for carcinogenic properties (i.e. chronic toxicity or bioassay studies), previous experience with a wide range of phthalates suggests that high doses might produce liver changes in rodents, but these are not relevant to humans and not indicative of a potential human risk. Three chronic toxicity/carcinogenicity studies of DINP have been conducted; two in rats and one in the mouse. In the rat studies, the major findings were liver and kidney changes principally related to the induction of peroxisome proliferation. There was an increase in liver tumors in both male and female rats and also a small increase in kidney tumors in the male rats. Both of these tumors are considered to be rat specific and without relevance to humans. In the mouse study, there were liver tumors as well, also the consequence of peroxisomal proliferation, but no tumors of other types.

Although not all members of the category have been tested for reproductive toxicity, (di-phC10 PE - CAS RN 53306-54-0, di-C11 PE - CAS RN 85507-79-5 or 3648-20-2, or di-C13 PE - CAS RN 68515-47-9), there are data for the lower (di-C7-9 PE - CAS RN 68515-41-3), intermediate (di-C9-11 PE - CAS RN 68515-43-5) and higher (di-C13 PE - CAS RN 119-06-2) molecular weight representatives that have shown no significant reproductive toxicity at doses up to 500 mg/kg/day or 250 mg/kg/day (di-C13 PE). Effects included transiently decreased body weights or slightly decreased ovary and epididymal weights. These effects are minor and are not directly related to reproductive toxicity. Furthermore, category members di-C7-9 PE and di-C9-11 PE have been recently shown not to be associated with detectable reproductive effects and do not affect fertility, similarly to DINP and DIDP.

Data from the developmental toxicity tests for the HMWPE conducted in rats, on di-phC10, di-C7-9, di-C9-11, and di-C13 PEs, have shown minimal maternal toxicity, at doses up to 1,000 mg/kg/day (limit dose) or 250 mg/kg/day (in di-C13 PE). Either no effects were produced or the effects were associated with decreased food consumption and body weight loss in dams. Only the di-phC10 PE showed maternal toxicity at the limit dose and associated effects of resorptions, decreased litter size, or fetal survival associated with the above two symptoms of maternal toxicity. In the two-generation study on DIDP, a decrease in offspring survival, more marked in F2, was observed. In the di C13 PE (CAS RN 119-06-2) 1 generation study (F1 generation) a decrease in survival indices was observed leading to a NOAEL of 50 mg/kg/day for offspring rats whereas NOAELs for parental rats were 250 mg/kg. These may be considered related to developmental effects. No such changes were seen in either generation of the separate studies on di-C7-9 PE and di-C9-11 PE; these results are consistent with results from DIDP studies.

However, none of the HMWPE substances tested produced developmental effects. Increased frequencies of developmental variants including dilated renal pelvis and supernumerary lumbar ribs were produced in the studies on di-C7-9 PE and di-C9-11 PE, but are common findings in rats. Although not all members of the HMWPE Category have been tested for developmental toxicity, there are data for the lower (di-phC10 and di-C7-9), intermediate (di-C9-11) and higher (di-C13) molecular weight representatives. Like DINP and DIDP, they have shown no significant developmental toxicity. It is reasonable to conclude that other members of the category would behave similarly, as shown by the weight of evidence. Thus, it can be concluded that this category of HMWPE induces no biologically significant developmental effects in rodents.

In conclusion, as demonstrated in the SIAR (sections 3.1.2 to 3.1.8), the weight of evidence shows that members of the HMWPE Category have a low order of acute and subchronic toxicity. They are not irritating to the skin or eyes. They are not skin sensitizers. They are not mutagenic. No or only minimal developmental toxicity and no adverse effects on reproductive capability have been observed in rodent studies. Thus, there is minimal concern about those PEs resulting in reproductive toxicity in humans.Although not tested for carcinogenicity, the members of this category do not show the potential for producing genetic effects. Also, the same mechanism of action through peroxisome proliferation can be anticipated for induction of liver tumors in rodents, and this is presumed not to be relevant to humans.

The results were consistent for all members of HMWPE Category in all endpoints and the toxicity has been well characterized. No further studies are proposed.

Environment

Members of the HMWPE Category are liquid at 25°C. Most of their physico-chemical properties were obtained by calculation using chemical structures that best characterize the range of constituent chemicals. They demonstrate relatively similar properties or progressive change across a range of values with melting point ranging from -48°C to -9°C, boiling point ranging from 398°C to 501°C (at 1,013 hPa), density ranging from 0.950g/cm^3 to 0.965 g/cm^3, vapour pressure ranging from 3.63E-10 hPa to 9.33E10-7 hPa at 25°C, water solubility values less than 0.0001 mg/l, and log P_{ow} values cited as greater than 6 and ranging up to 12.1.

Results of distribution modeling, using a Mackay Level I model, suggest that members of the HMWPE Category will partition primarily to the soil compartment (approximately 98%) with a small amount partitioning to sediment (approximately 2%). Volatilization to air from aqueous and terrestrial habitats will be negligible because category members have low vapor pressure (<9.33E-7 hPa at 25°C). However, the small fraction that may partition to air has the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals with calculated degradation half-lives ranging from approximately 4 to 7 hours depending on hydroxyl radical concentration. Aqueous photolysis and hydrolysis will not contribute to the transformation of phthalate esters in aquatic environments because they are poorly or not susceptible to these reactions. Hydrolysis half-lives of >3 years are estimated for category members.

Members of the HMWPE Category have the potential to biodegrade from 12.8% to 75% biodegradation within 28 days, in ready biodegradability tests. Members of the category, as well as DIDP, have not been shown to be readily biodegradable. Although the two highest molecular weight members of this category, di-C13 PEs with CAS RN 119-06-2 and 68515-47-9, exhibited lower relative extents of biodegradability at 28 days when compared to the other category members, the extant database for these substances show that they can be biodegraded to levels similar to the other lower molecular weight members of this category over an extended test duration (56 days). Data for DINP show that it is readily biodegradable within 28 days. Additionally, studies show that HMWPEs do not inhibit microbial respiration in terrestrial and sewage systems. Category members are expected to sorb to organic matter in soil, sediment, and wastewater solids based on calculated log K_{oc} values that range between 4.5 and 7.7.

The acute and chronic aquatic toxicity of HMWPEs has been evaluated using numerous species. These data clearly show that category members do not exhibit acute and chronic aquatic toxicity at or below their maximum attainable water solubility. The solubility of these substances is equal to or less than 0.017 mg/L. As such, aqueous exposure to these substances will be very limited.

Concerning terrestrial environments, the compartment of primary interest as indicated by partitioning data, studies on members of the HMWPE Category are not available. However, they are not expected to exhibit toxicity based on results from earthworm studies for an analog substance, DIDP, which was applied at a concentration as high as 7,994 mg/kg soil, dry weight. The two lower molecular weight category members, di-C7-9 PE and di-C9-11 PE, may cause effects in plants at very high concentrations, greater than 8,000 mg/kg soil, dry weight, based on data for DINP, which contains constituents that can be found in the two category members. Results from sediment toxicity studies with two freshwater invertebrates that showed no effects at relatively high concentrations (up to 2,900 mg/kg sediment, dry weight) suggest that category members will not produce toxicity to sediment invertebrates. Although the phthalate esters tested, DINP, DIDP, and a di-C7-11 PE, do not belong to the HMWPE Category, select category member constituents have overlapping carbon number ranges and similar structures. Finally, it has been demonstrated that HMWPEs have a low potential to bioaccumulate in aquatic species, demonstrated by a food web study on DINP, and bioconcentration studies on DINP, DIUP and di-C13 PE . Metabolic transformation is the most likely reason why these substances exhibit decreasing concentrations from lower to higher trophic levels.

Exposure

Estimated European production is approximately 60 to 100k tonnes per year (European Council for Plasticisers and Intermediates - personal communication). This is likely to represent a third of world production.

HMWPEs are used primarily as industrial chemicals associated with polymers, mainly as additives to impart flexibility in polyvinyl chloride (PVC) resins, but are also used as synthetic base stocks for lubricating oils. Polymer applications can be divided into PVC-related uses and uses involving other non-PVC polymers. PVC-containing phthalate ester applications can include wire and cable insulating, furniture and automobile upholstery, flooring, wall coverings, coil coatings, pool liners, roofing membranes, and coated fabrics. Polymer containing phthalate ester applications that are non-PVC based, include thermoplastics, rubbers and selected paints and adhesives. Members of the HMWPE Category are not used for PVC-medical or toy applications. Due to their high viscosity, slow fusion and high costs, members of the HMWPE Category are not preferred for the manufacture of toys.

Essentially all HMWPEs released from their manufacture, which can occur when cleaning manufacturing systems, enter wastewater treatment facilities where they can be biodegraded or sorbed to sewage sludge.

The majority of HMWPEs found in the environment likely come from the slow release of these chemicals from phthalate ester-containing polymer products as a result of weathering processes. Once phthalates are produced and used in various products, emissions can occur during the end-use of these products. Unlike industrial point sources, emissions during product end-use represent a diffuse emission source. In both polymer uses the phthalate ester serves as a plasticiser that enhances the flexibility of the product as a result of the positioning of the phthalate ester molecules between the polymer chains. However, since the phthalate ester molecules are not covalently bound to the polymer matrix, user or consumer exposure, or migration and subsequent release to the environment may occur. Since most HMWPEs are sandwiched within a polymer matrix, emissions are retarded during the life of the polymer product.

Exposure to HMWPEs may occur at workplaces where they are manufactured. Based on physical properties, the primary workplace exposure in production activities would be dermal and there may be a potential for formation of aerosols during some applications. However, HMWPEs are handled only in industrial manufacturing facilities and the majority of the applications involve incorporation of the phthalate ester into a matrix. Therefore, minimal consumer exposure is foreseen, since the consumer is only indirectly exposed through the use of products, which may contain HMWPEs and uptake is expected to be low.

RECOMMENDATIONS

The chemicals in this category are currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemicals possess properties indicating a low hazard for human health and the environment. Therefore, members of the HMWPE Category are currently of low priority for further work because of their low hazard profile.